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Hydrogel: A class of polymeric materials

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ABSTRACT

A class of polymeric materials known as hydrogel products have a hydrophilic structure that allows them to store enormous amounts of water in their three-dimensional networks. More than any other form of synthetic biomaterial, they most nearly resemble genuine living tissue because of their high water content, porosity, and soft consistency. Hydrogels may also be prepared into a wide range of physical forms, such as coatings, films, microparticles, and slabs. Hydrogels are so often utilized in clinical practice and medicine for a variety of purposes, such as cellular immobilization, tissue engineering and regenerative medicine, diagnostics, separation of biomolecules or cells, and barrier materials to control biological adhesions. This biomaterial has the capacity to expand and store huge volumes of biological fluids. They are mushy when swollen⁷.

Keywords: Hydrogel; cross-linking; polymer; hydrogel properties

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INTRODUCTION

Polymer hydrogels are a class of polymers that are evolving quickly and have various uses in a variety of industries, particularly in agriculture, medicine, and pharmacy. Numerous studies on the novel characteristics, chemical and physical architectures, and inventive, constrained uses of polymer hydrogels have been published. They are hydrophilic, three-dimensional, polymeric networks with swelling properties that can retain a lot of water without losing their structural integrity⁵¹.

Their crosslinking network structure, which is created by hydrophilic groups containing polymers like -OH, -CONH, -COOH, -SO₃H, and -NH₂, is what allows them to absorb water. The macromolecular architectures that may be found in both chemical and physical hydrogels are diverse. These comprise hydrophilic networks stabilized by hydrophobic domains, IPNs or physical blends, polyion-multivalent ion, polyion-polyion, or H-bonded complexes, and cross-linked or entangled networks of linear homopolymers, linear copolymers, and block or graft copolymers.

Hydrogels can also take on several physical shapes, as seen in table

Physical forms	Examples
Solid molded forms	Soft contact lenses
Pressed powder matrices	Pills or capsules for oral ingestion
Microparticles	As bio adhesive carriers or wound treatment
Coatings	On implants or catheters; on pills or capsules; or coatings on the inside capillary wall in capillary electrophoresis
Membranes or sheets	As a reservoir in a transdermal drug delivery patch; or for 2D electrophoresis gels
Encapsulated solids	As a osmotic pumps
Liquids	That form gels on heating or cooling

Polysaccharides, one of the many polymers that have been suggested for hydrogel synthesis, offer several benefits over synthetic polymers, which were first used in the pharmaceuticals industry. In fact, polysaccharides are widely available and derived from enable sources such microbial cultures of specific strains, plant and algae kingdoms, and recombinant DNA processes. Natural or synthetic polymers can be used to create or synthesize them. Despite the possibility of pathogens, inadequate mechanical properties, and inflammatory or immune reactions, hydrogels derived from natural polymers offer several benefits, including inherent biocompatibility, biodegradability, and biologically identifiable moieties that facilitate cellular functions.

These intrinsic biological characteristics are not present in synthetic hydrogels. Thankfully, synthetic polymers often include distinct structures that may be altered to provide customized functionality and degradability. Plant-derived polymers are specifically used in pharmaceutical

formulations to make solid monolithic matrix systems, implants, films, beads, microparticles, and injectable and inhalable systems.

Characteristic of hydrogen³

1. Its maximum absorbance under load (AUC) and rewetting capacity are expected.
2. They have low solubility and minimal residual manners.
3. It is highly stable and durable in an environment that expands when stored.
4. It has the highest photo stability in nature and is colorless, odorless, and nontoxic.
5. When placed in swelling media, hydrogel needs to have the best biodegradability and pH neutrality.
6. The drug ought to have a molecular weight of no more than 500 Daltons and appropriate hydrophilicity.
7. The drug's PH value ranges from 5 to 9.
8. The medicine has to have a high acidic or alkaline solution; otherwise, it cannot be used with a topical drug delivery method

Advantages^{5,3}

1. Since hydrogels have a great water-holding capacity and some degree of flexibility, they are homogeneous to natural tissue.
2. Along with having good transport qualities, it should be biodegradable and biocompatible.
3. It might not be too harmful.
4. Hydrogels are easily modifiable and injectable.
5. It is capable of varying temperature, concentration, and pH.

Disadvantages^{5,3}

1. Limitation of hydrogels in contact lenses is hypoxia, dehydration, lenses deposition and red eye reactions.
2. It ought to be non-adherent, difficult to sterilize, and challenging to fill with nourishment or medications.
3. It may be expensive.
4. Its mechanical strength is modest.
5. Managing it might be challenging.

Classification of hydrogel^{51,3}

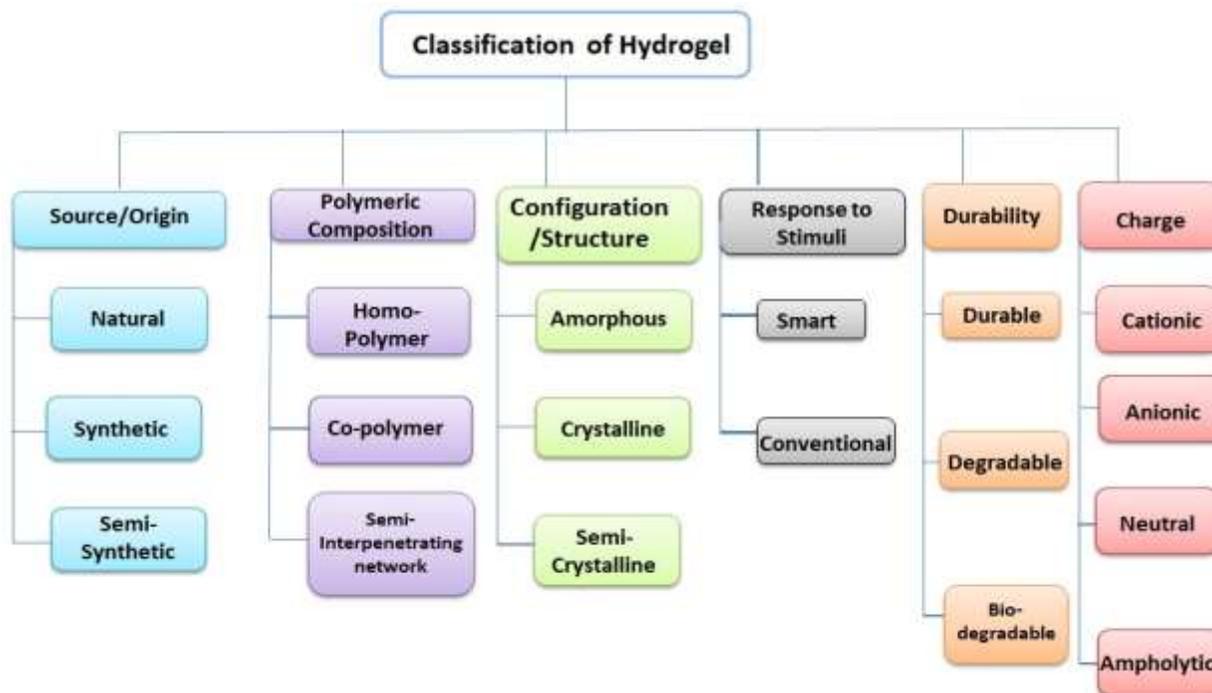


Figure 1: Schematic diagram of most common classes of hydrogels.

➤ **Classification based on source**

- There are two types of hydrogel: those with a natural origin and those with a synthetic origin.

➤ **Classification based on the polymeric composition/ Method of preparation**

- Hydrogels made of homopolymeric polymers are referred to as polymeric networks that originate from a single species of monomer. The cross-linked skeletal structure of these hydrogels is dependent on the kind of monomers and polymerization process used.
- Copolymeric hydrogels: These are hydrogels made of several monomers, each of which contains a single hydrophilic component.
- Polymer Two separate natural or synthetic polymer components make up interpenetrating polymeric hydrogels (IPN). One polymer in this kind of categorization is a noncross-linked polymer network.

➤ **Classification based on the configuration/ physical structure of the network**

- These hydrogels can be categorized as amorphous (non-crystalline), semi crystalline, hydrogen bonded, super molecular structure, or hydro colloidal aggregation based on their physical structure and chemical makeup.

➤ **Classifications based on the physical appearance**

- Hydrogels can take the form of films, matrices, or microspheres, depending on how they are polymerized.

➤ **Classifications based on the type of the cross linking**

- Hydrogels may be classified into two groups based on the kind of cross-linking: chemical and physical.
- Chemical connecting, in which both junctions are ionic contacts, hydrogen bonds, or hydrophobic interactions, is permanent compared to physical linking, which is the transitory junction.

➤ **Classifications based on the network electrical charges/ ionic charges**

- Hydrogels fall into four groups based on whether or not they have electrical charges: ionic (anionic or cationic), non-ionic (neutral), amphoteric electrolytes (ampholytic), and zwitter ionic.

➤ **Based on the mechanical controlling the drug release**

- It involves a release system that is chemically regulated, diffusion controlled, swelling controlled, and environment sensitive.

METHOD OF PREPARATION: - ^{1,2,3,7}

Hydrophilic polymer networks are called hydrogels. Hydrophilic and hydrophobic monomers are sometimes used in the manufacture of hydrogels to control the properties of certain applications. Using copolymerization or cross-linking free-radical polymerization, hydrophilic monomers and multifunctional cross-linkers can react to form hydrogels. Water solubility linear polymers of natural and synthetic origin have been combined to form hydrogels in several ways:

- Using ionizing radiation to generate main-chain free radicals which can recombine as cross-link junctions.
- Linking polymer chains via chemical reaction.
- Physical interactions such as entanglements, electrostatics, and crystallite formation.

The creation of hydrogels generally involves three essential components: the monomer, the initiator, and the cross-linker.

Bulk polymerization:- ^{2,3}

One or more types of monomers can be used to create bulk hydrogels; vinyl monomers are the most common type used in hydrogel manufacturing. Any hydrogel formulation typically includes a minor addition of crosslinking agent. To start the polymerization reaction, one can utilize radiation, ultraviolet light, or chemical catalysts. The type of solvents and monomers being employed determines which initiator is used. Numerous shapes and sizes of the polymerized hydrogel can be created, such as rods, particles, films, membranes, and emulsions.

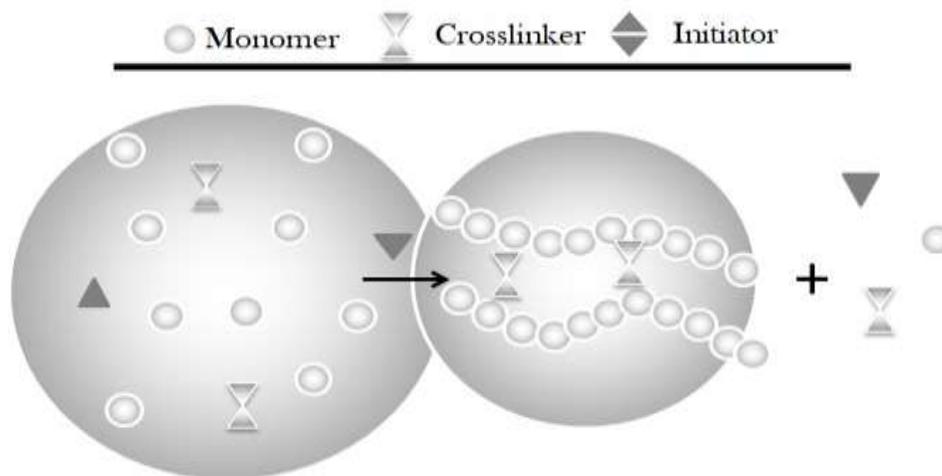


Figure 2 Schematic diagram of hydrogel preparation 7

Free radical polymerization: ^{3,7,43}

In this process, acrylates, vinyl lactams, and amides are the primary monomers used to make hydrogels. These polymers are functionalized with groups that are radically polymerizable or have appropriate functional groups. The initiation, termination, propagation, and chain transfer chemistry of common free radical polymerizations are all included in this technique. An extensive range of thermal, UV, visible, and redox initiators can be used for the radical formation in the initiation stage; the radicals react with the monomers to transform them into active forms.

Solution polymerization/cross-linking: ^{2,13}

In these, the multifunctional crosslinking agent is used with neutral or ionic monomers. A redox initiator system or UV radiation are two thermal methods of starting the polymerization process. Having a solvent present to act as a heat sink is a major benefit of solution polymerization over bulk polymerization. The hydrogels that have been created undergo a washing process using distilled water in order to eliminate any contaminants such as extractable polymer, soluble monomers, oligomers, cross-linking agent, etc. Water-ethanol blends, ethanol, water, and benzyl alcohol were employed as solvents.

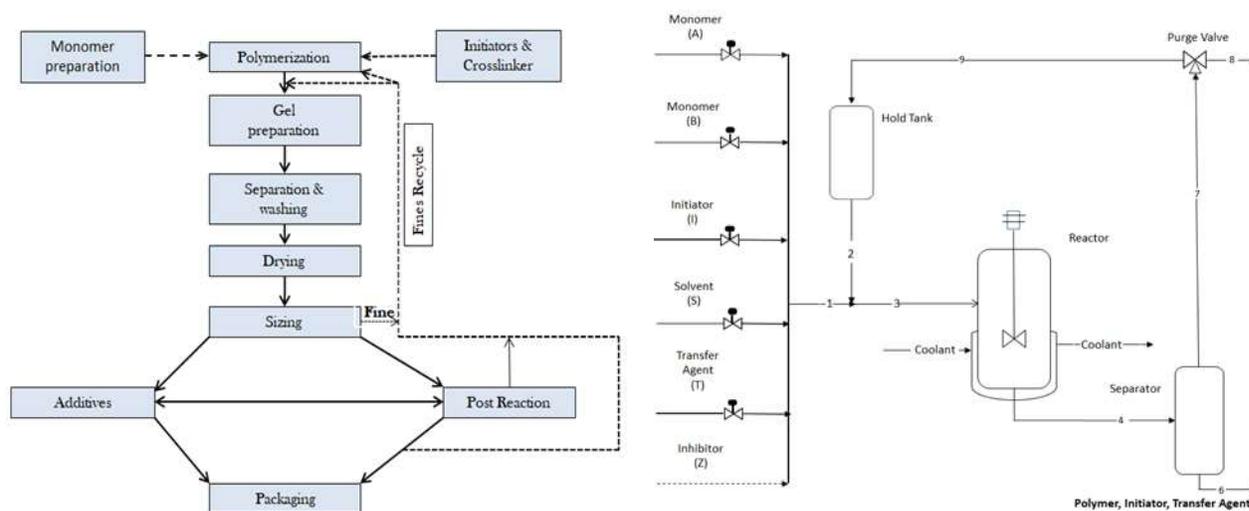


Figure 3 A-Hydrogel preparation block diagram (solution polymerization/cross-linking procedure) and Figure 3 B- Solution polymerization with recycle loop.2, 3

Suspension polymerization or inverse-suspension polymerization: - 3,4,7

One benefit of this process is that it produces goods in the form of powder or microspheres, or beads, negating the need for grinding. The polymerization process is known as "inverse suspension" since the water-in-oil (W/O) method is selected rather than the more popular oil-in-water (O/W) method. Using this method, a homogenous mixture of the monomers and initiator is distributed throughout the hydrocarbon phase. The rotor design, agitation speed, dispersant type, and monomer solution viscosity are all controlled by the size and form of the resin particles. Due to its thermodynamic instability, the dispersion needs to be constantly stirred in addition to having a low hydrophilic-lipophilic balance (HLB) suspending agent added.

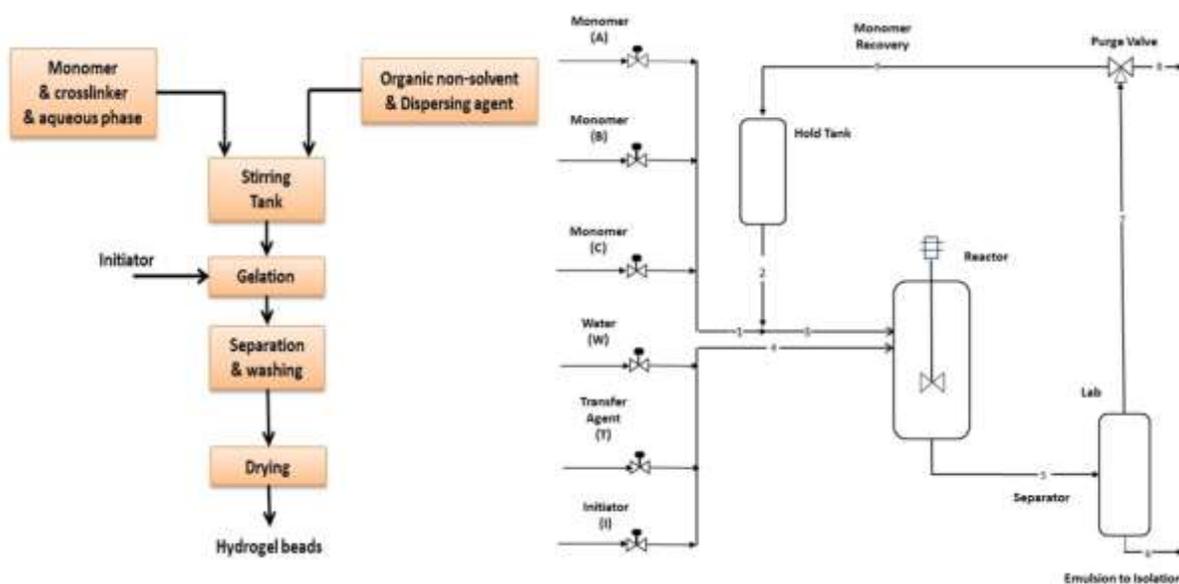


Figure 4: Suspension polymerization with recycle loop 19

Grafting to a support:^{3,7}

It is essential to strengthen a hydrogel's mechanical characteristics in order to graft it onto a stronger support, as hydrogels made through bulk polymerization have a weaker structure. In order to construct a chain of monomers that are covalently bound to the support, free radicals must first be generated onto a stronger support surface, after which monomers must be polymerized directly onto it.

Polymerization by irradiation:-^{2,3,7}

Initiators such as ionizing high energy radiation, such as gamma rays and electron beams, have been employed to create hydrogels of unsaturated molecules. Radicals are created on the polymer chains as a result of radiation applied to an aqueous polymer solution. A cross-linked structure is ultimately created as a result of the macro-radicals recombining on various chains to form covalent bonds. UV polymerization is performed using poly (vinyl alcohol), poly (ethylene glycol), and poly (acrylic acid). This process yields hydrogels that are comparatively pure and initiator-free.

Physical cross-linking:-^{3,7}

By physically connecting polymers, it is the most popular and straightforward method for creating hydrogels.

The interaction of ions involved in this physical cross-linking includes hydrophobic association, polyelectrolyte complexation, and hydrogen bonding. The different techniques for creating physically cross-linked hydrogels are as follows:

Heating/cooling a polymer solution:-

In order to create physically cross-linked gels, heated solutions of gelatin or carrageenan are cooled. The helical association, helix creation, and developing junction zones are what cause the gel to form. Polyethylene glycol-poly(lactic acid) hydrogel and polyethylene oxide-polypropylene oxide are two examples.

Complex coacervation:-

Polyanions and polycations combined to form complicated coacervate gels. This method's basic idea is that, depending on the concentration and pH of the corresponding solutions, polymers with opposite charges will cling to one another and create soluble or insoluble complexes. Coacervating polyanionic xanthan with polycationic chitosan is one instance of this.

Ionic interaction:-

Cross linking between polymers occurs when di- or trivalent counter ions are added to an ionic polymer. The idea behind this technique is to combine a multivalent ion with opposite charges

(like $\text{Ca}^{2+} + 2\text{Cl}^-$) with a polyelectrolyte solution (like Na^+ alginate-). Chitosan-polylysine, chitosan-glycerol phosphate salt, and chitosan dextran hydrogels are a few more examples.

Hydrogen Bonding:

A functional group with a high electron density joins forces with an electron-deficient hydrogen atom to form a hydrogen bond. For instance, the creation of hydrogen bonds between PA and PNVP can result in a hydrogel. The molar ratio of each polymer, polymer concentration, solvent type, solution temperature, and polymer structure are the variables that impact the hydrogels.

Chemical cross-linking:

In this procedure, two polymer chains are linked together by a crosslinking agent, and monomers are grafted onto the polymers' backbones. When functional groups in natural and synthetic polymers, including OH, COOH, and NH_2 , combine with cross-linkers like aldehyde (like glutaraldehyde and adipic acid dihydrazide), cross-linking of the polymers is produced. In order to create an interpenetrating network structure, IPN is a polymerized monomer inside another solid polymer.

Application of hydrogels in drug delivery³

Hydrogels have garnered significant interest as superior options for targetable therapeutic agent devices, controlled release devices, and bioadhesive devices. Hydrogel-based delivery systems can be used subcutaneously, topically, ocular, rectal tract, or orally. There are several locations where hydrogels can be used to deliver drugs.

- **Drug delivery in the oral cavity:**

A medication is mixed into hydrogels and administered locally to the oral cavity to treat conditions including stomatitis, fungal infections, periodontal disease, viral infections, and malignancies of the oral cavity.

- **Drug delivery in the GI tract:**

GI tract is the most popular route of drug delivery because of the facility of administration of drugs for compliant therapy, and its large surface area for systemic absorption. Like buccal delivery, hydrogel-based devices can be designed to deliver drugs locally to the specific sites in the GI tract. For example, stomach-specific antibiotic drug delivery systems for the treatment of *Helicobacter pylori* infection in peptic ulcer disease.

- **Wound healing:**

Hydrogels' cross-linked nature gives them the capacity to contain both drugs and water. Wound exudates can be held and retained by them because of their capacity to hold water.

When administered, hydrogels based on gelatin and sodium alginate can shield the site from bacterial infection.

- **Hydrogels for brain:**

Like other barriers in the human body, the blood-brain barrier presents a hurdle for medication delivery. Approximately 98% of newly synthesized medicines are unable to pass this barrier. As a result, there aren't many medications available for CNS drug delivery. Rats were seen to be loaded with PLGA microspheres by the long-term sustained release medication camptothecin. Rats with malignant gliomas have a longer life span when these microspheres are present.

- **Rectal delivery:**

Drugs absorbed from the lower portion of the rectum are known to immediately enter the systemic circulation. For the delivery of drugs with first pass metabolism, the rectal route is therefore helpful. Its main uses have been in the local treatment of rectum-related conditions including hemorrhoids.

- **Ocular drug delivery:**

The most common application for hydrogels is in ocular medication delivery systems. The majority of hydrogel films made of polymers are used to make both hard and soft contact lenses. The long-term retention of in-situ forming hydrogels as a gel following dosage and their ease of dosing as a liquid make them appealing as an eye medication delivery strategy.

- **Subcutaneous Delivery:**

Because hydrogels naturally degrade, we can create implantable hydrogels that are also biodegradable. Cross-linked PHEMA, which is applied to cytarabine, is being produced for use in the subcutaneous administration of anticancer medicines.

- **Transdermal Delivery:**

Drugs can be delivered transdermally using a variety of hydrogel-based drug delivery devices. The field of wound dressing can benefit from the use of swollen hydrogels as controlled release agents. In order to achieve improved product penetration such as for hormones and nicotine hydrogel-based formulations for transdermal iontophoresis are being investigated.

- **Topical drug delivery:**

Active ingredients like desonide, a synthetic corticosteroid often used as an anti-inflammatory, have been delivered via hydrogels. Since the hydrogels' moisturizing

qualities were designed to improve patient compliance, scaling and dryness are not anticipated with this medication administration method.

CONCLUSION:

In order to satisfy the demands of various applications, several hydrogel-based networks have recently been created and customized.

These hydrogels have the capacity to either swell when placed in contact with an aqueous solution. The current study provides information on the many bases on which hydrogels are classified, as well as their physical and chemical properties, technological viability, preparation process, and application methods. The study reveals that hydrogels possess remarkable qualities that will enable them to be widely used as the next generation of biomaterials. Hydrogels are thus also referred to as smart or intelligent biomaterials. Hydrogels can be made using a variety of current technologies. This page discusses a few of them.

FUTURE PROSPECT:

The problem of both acute and chronic wounds has negatively impacted society and the economy; in order to address these negative impacts, significant changes in healthcare are necessary. There are several issues with the existing wound healing treatments that prolong recovery. To address these inadequacies, a new and enhanced system is therefore required. Because of their perfect qualities such as preserving a moist environment, absorbing exudates and necrotic tissue, and being flexible enough to cover wounds with varying morphologies—hydrogels have been recommended as suitable wound dressings for both acute and chronic wounds. Hydrogels are composed of either synthetic or natural polymers; a balance of the two is best for creating blended hydrogels with properties that promote wound healing. Sprayable hydrogels are part of the upcoming wave of wound dressings.

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